



SEQUENCE LISTING

#6

<110> WOLFMEIER
KHOR, SOO-PEANG

<120> MODIFIED AND STABILIZED GDF PROPEPTIDES AND USES THEREOF

<130> 08702-0100-00000

<140> 10/071,499

<141> 2002-02-08

<160> 16

<170> PatentIn version 3.1

<210> 1

<211> 375

<212> PRT

<213> Homo sapiens

<400> 1

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
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Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu Asn
20 25 30

Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn Thr
35 40 45

Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys Leu
50 55 60

Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln Leu
65 70 75 80

Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val
85 90 95

Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His
100 105 110

Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe Leu
115 120 125

Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser Ser
 130 135 140

Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr Leu
 145 150 155 160

Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg Leu
 165 170 175

Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser Leu
 180 185 190

Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val
 195 200 205

Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly
 210 215 220

Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr
 225 230 235 240

Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys
 245 250 255

Val Thr Asp Thr Pro Lys Arg Ser Arg Arg Asp Phe Gly Leu Asp Cys
 260 265 270

Asp Glu His Ser Thr Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val
 275 280 285

Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr
 290 295 300

Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu Phe Val Phe Leu Gln Lys
 305 310 315 320

Tyr Pro His Thr His Leu Val His Gln Ala Asn Pro Arg Gly Ser Ala
 325 330 335

Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr
 340 345 350

Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ala Met Val

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Val Asp Arg Cys Gly Cys Ser
370 375

<210> 2
<211> 1125
<212> DNA
<213> Homo sapiens

<400> 2
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gtggatctaa atgagaacag tgagcaaaaa gaaaatgtgg aaaaagaggg gctgtgtaat 120
gcatgtactt ggagacaaaa cactaaatct tcaagaatag aagccattaa gatacaaatc 180
ctcagtaaac ttcgtctgga aacagctcct aacatcagca aagatgttat aagacaactt 240
ttacccaaag ctccctccact ccgggaactg attgatcagt atgatgtcca gagggatgac 300
agcagcgatg gctctttgga agatgacgat tatcacgcta caacggaaac aatcattacc 360
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tccaacttag gcattgaaat aaaagcttta gatgagaatg gtcattgatct tgctgtaacc 720
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tgctgtcggt accctctaac tgtggatttt gaagcttttg gatgggattg gattatcgct 900
cctaaaagat ataaggccaa ttactgctct ggagagtgtg aatttgtatt ttacaaaaa 960
tatcctcata ctcatctggg acaccaagca aaccccagag gttcagcagg cccttgctgt 1020
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<210> 3
<211> 109
<212> PRT
<213> Homo sapiens

<400> 3

Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg Cys Cys
 1 5 10 15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
 20 25 30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu
 35 40 45

Phe Val Phe Leu Gln Lys Tyr Pro His Thr His Leu Val His Gln Ala
 50 55 60

Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
 65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly
 85 90 95

Lys Ile Pro Ala Met Val Val Asp Arg Cys Gly Cys Ser
 100 105

<210> 4
 <211> 327
 <212> DNA
 <213> Homo sapiens

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 aattactgct ctggagagtg tgaatttgta tttttacaaa aatatcctca tactcatctg 180
 gtacaccaag caaacccag aggttcagca ggcccttgct gtactccac aaagatgtct 240
 ccaattaata tgctatattt taatggcaaa gaacaaataa tatatgggaa aattccagcg 300
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<210> 5
 <211> 243
 <212> PRT
 <213> Homo sapiens

<400> 5

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 1 5 10 15

Asn Ala Cys Thr Trp Arg Gln Asn Thr Lys Ser Ser Arg Ile Glu Ala

20

25

30

Ile Lys Ile Gln Ile Leu Ser Lys Leu Arg Leu Glu Thr Ala Pro Asn
 35 40 45

Ile Ser Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu
 50 55 60

Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp
 65 70 75 80

Gly Ser Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile
 85 90 95

Thr Met Pro Thr Glu Ser Asp Phe Leu Met Gln Val Asp Gly Lys Pro
 100 105 110

Lys Cys Cys Phe Phe Lys Phe Ser Ser Lys Ile Gln Tyr Asn Lys Val
 115 120 125

Val Lys Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Glu Thr Pro Thr
 130 135 140

Thr Val Phe Val Gln Ile Leu Arg Leu Ile Lys Pro Met Lys Asp Gly
 145 150 155 160

Thr Arg Tyr Thr Gly Ile Arg Ser Leu Lys Leu Asp Met Asn Pro Gly
 165 170 175

Thr Gly Ile Trp Gln Ser Ile Asp Val Lys Thr Val Leu Gln Asn Trp
 180 185 190

Leu Lys Gln Pro Glu Ser Asn Leu Gly Ile Glu Ile Lys Ala Leu Asp
 195 200 205

Glu Asn Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro Gly Glu Asp
 210 215 220

Gly Leu Asn Pro Phe Leu Glu Val Lys Val Thr Asp Thr Pro Lys Arg
 225 230 235 240

Ser Arg Arg

<210> 6
 <211> 729
 <212> DNA
 <213> Homo sapiens

<400> 6
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 tggagacaaa aactaaatc ttcaagaata gaagccatta agatacaaat cctcagtaaa 120
 cttcgtctgg aaacagctcc taacatcagc aaagatgtta taagacaact ttaccctaaa 180
 gctcctccac tccgggaact gattgatcag tatgatgtcc agagggatga cagcagcgat 240
 ggctctttgg aagatgacga ttatcacgct acaacggaaa caatcattac catgcctaca 300
 gagtctgatt ttctaattgca agtggatgga aaacccaaat gttgcttctt taaatttagc 360
 tctaaaatac aatacaataa agtagtaaag gcccaactat ggatatattt gagaccgctc 420
 gagactccta caacagtgtt tgtgcaaata ctgagactca tcaaacctat gaaagacggc 480
 acaagggtata ctggaatccg atctctgaaa cttgacatga acccaggcac tggatatttgg 540
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 ggcattgaaa taaaagcttt agatgagaat ggtcatgatc ttgctgtaac cttcccagga 660
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 tccagaagg 729

<210> 7
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 <212> PRT
 <213> Homo sapiens

<400> 7

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
 1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala Ala Glu Gly Pro Ala Ala Ala Ala
 20 25 30

Ala Ala Ala Ala Ala Ala Ala Ala Ala Gly Val Gly Gly Glu Arg Ser
 35 40 45

Ser Arg Pro Ala Pro Ser Val Ala Pro Glu Pro Asp Gly Cys Pro Val
 50 55 60

Cys Val Trp Arg Gln His Ser Arg Glu Leu Arg Leu Glu Ser Ile Lys
65 70 75 80

Ser Gln Ile Leu Ser Lys Leu Arg Leu Lys Glu Ala Pro Asn Ile Ser
85 90 95

Arg Glu Val Val Lys Gln Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln
100 105 110

Ile Leu Asp Leu His Asp Phe Gln Gly Asp Ala Leu Gln Pro Glu Asp
115 120 125

Phe Leu Glu Glu Asp Glu Tyr His Ala Thr Thr Glu Thr Val Ile Ser
130 135 140

Met Ala Gln Glu Thr Asp Pro Ala Val Gln Thr Asp Gly Ser Pro Leu
145 150 155 160

Cys Cys His Phe His Phe Ser Pro Lys Val Met Phe Thr Lys Val Leu
165 170 175

Lys Ala Gln Leu Trp Val Tyr Leu Arg Pro Val Pro Arg Pro Ala Thr
180 185 190

Val Tyr Leu Gln Ile Leu Arg Leu Lys Pro Leu Thr Gly Glu Gly Thr
195 200 205

Ala Gly Gly Gly Gly Gly Gly Arg Arg His Ile Arg Ile Arg Ser Leu
210 215 220

Lys Ile Glu Leu His Ser Arg Ser Gly His Trp Gln Ser Ile Asp Phe
225 230 235 240

Lys Gln Val Leu His Ser Trp Phe Arg Gln Pro Gln Ser Asn Trp Gly
245 250 255

Ile Glu Ile Asn Ala Phe Asp Pro Ser Gly Thr Asp Leu Ala Val Thr
260 265 270

Ser Leu Gly Pro Gly Ala Glu Gly Leu His Pro Phe Met Glu Leu Arg
275 280 285

Val Leu Glu Asn Thr Lys Arg Ser Arg Arg Asn Leu Gly Leu Asp Cys

290		295		300
Asp Glu His Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val				
305		310		315 320
Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr				
	325		330	335
Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu Tyr Met Phe Met Gln Lys				
	340		345	350
Tyr Pro His Thr His Leu Val Gln Gln Ala Asn Pro Arg Gly Ser Ala				
	355		360	365
Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr				
	370		375	380
Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly Lys Ile Pro Gly Met Val				
385		390		395 400
Val Asp Arg Cys Gly Cys Ser				
	405			

<210> 8
 <211> 1221
 <212> DNA
 <213> Homo sapiens

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gcgggggtcg ggggggagcg ctccagccgg ccagccccgt ccgtggcgcc cgagccggac	180
ggctgccccg tgtgcgtttg gcggcagcac agccgcgagc tgcgcctaga gagcatcaag	240
tcgcagatct tgagcaaact gcggctcaag gaggcgcca acatcagccg cgaggtggtg	300
aagcagctgc tgcccaaggc gccgccgctg cagcagatcc tggacctaca cgacttccag	360
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accgtcatta gcatggccca ggagacggac ccagcagtac agacagatgg cagccctctc	480
tgctgccatt ttcacttcag cccaaggtg atgttcacaa aggtactgaa ggcccagctg	540
tgggtgtacc tacggcctgt accccgcca gccacagtct acctgcagat cttgcgacta	600


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aaaccctaa ctggggaagg gaccgcaggg ggagggggcg gaggccggcg tcacatccgt      660
atccgctcac tgaagattga gctgcactca cgctcaggcc attggcagag catcgacttc      720
aagcaagtgc tacacagctg gttccgccag ccacagagca actggggcat cgagatcaac      780
gcctttgatc ccagtggcac agacctggct gtcacctccc tggggccggg agccgagggg      840
ctgcatccat tcatggagct tcgagtccta gagaacacaa aacgttcccg gcggaacctg      900
ggctctggact gcgacgagca ctcaagcgag tcccgcgtgct gccgatatcc cctcacagtg      960
gactttgagg ctttcggctg ggactggatc atcgcaccta agcgctacaa ggccaactac     1020
tgctccggcc agtgcgagta catgttcatg caaaaatatc cgcataccca tttggtgcag     1080
caggccaatc caagaggctc tgctggggcc tgttgtagcc ccaccaagat gtccccaatc     1140
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gtggatcgct gtggctgctc t                                     1221

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<210> 9
<211> 109
<212> PRT
<213> Homo sapiens

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<400> 9

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Asn Leu Gly Leu Asp Cys Asp Glu His Ser Ser Glu Ser Arg Cys Cys
1          5          10          15

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Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
          20          25          30

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Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu
          35          40          45

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Tyr Met Phe Met Gln Lys Tyr Pro His Thr His Leu Val Gln Gln Ala
          50          55          60

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Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65          70          75          80

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Pro Ile Asn Met Leu Tyr Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly
          85          90          95

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Lys Ile Pro Gly Met Val Val Asp Arg Cys Gly Cys Ser
          100          105

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<210> 10
 <211> 327
 <212> DNA
 <213> Homo sapiens

<400> 10
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 aactactgct ccggccagtg cgagtacatg ttcatgcaaa aatatccgca taccatttg 180
 gtgcagcagg ccaatccaag aggctctgct gggccctgtt gtacccccac caagatgtcc 240
 ccaatcaaca tgctctactt caatgacaag cagcagatta tctacggcaa gatccctggc 300
 atggtggtgg atcgctgtgg ctgctct 327

<210> 11
 <211> 274
 <212> PRT
 <213> Homo sapiens

<400> 11
 Ala Glu Gly Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala
 1 5 10 15
 Ala Gly Val Gly Gly Glu Arg Ser Ser Arg Pro Ala Pro Ser Val Ala
 20 25 30
 Pro Glu Pro Asp Gly Cys Pro Val Cys Val Trp Arg Gln His Ser Arg
 35 40 45
 Glu Leu Arg Leu Glu Ser Ile Lys Ser Gln Ile Leu Ser Lys Leu Arg
 50 55 60
 Leu Lys Glu Ala Pro Asn Ile Ser Arg Glu Val Val Lys Gln Leu Leu
 65 70 75 80
 Pro Lys Ala Pro Pro Leu Gln Gln Ile Leu Asp Leu His Asp Phe Gln
 85 90 95
 Gly Asp Ala Leu Gln Pro Glu Asp Phe Leu Glu Glu Asp Glu Tyr His
 100 105 110
 Ala Thr Thr Glu Thr Val Ile Ser Met Ala Gln Glu Thr Asp Pro Ala
 115 120 125

Val Gln Thr Asp Gly Ser Pro Leu Cys Cys His Phe His Phe Ser Pro
 130 135 140

Lys Val Met Phe Thr Lys Val Leu Lys Ala Gln Leu Trp Val Tyr Leu
 145 150 155 160

Arg Pro Val Pro Arg Pro Ala Thr Val Tyr Leu Gln Ile Leu Arg Leu
 165 170 175

Lys Pro Leu Thr Gly Glu Gly Thr Ala Gly Gly Gly Gly Gly Gly Arg
 180 185 190

Arg His Ile Arg Ile Arg Ser Leu Lys Ile Glu Leu His Ser Arg Ser
 195 200 205

Gly His Trp Gln Ser Ile Asp Phe Lys Gln Val Leu His Ser Trp Phe
 210 215 220

Arg Gln Pro Gln Ser Asn Trp Gly Ile Glu Ile Asn Ala Phe Asp Pro
 225 230 235 240

Ser Gly Thr Asp Leu Ala Val Thr Ser Leu Gly Pro Gly Ala Glu Gly
 245 250 255

Leu His Pro Phe Met Glu Leu Arg Val Leu Glu Asn Thr Lys Arg Ser
 260 265 270

Arg Arg

<210> 12
 <211> 822
 <212> DNA
 <213> Homo sapiens

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cagcccgagg acttcctgga ggaggacgag taccacgcca ccaccgagac cgtcattagc 360
 atggcccagg agacggaccc agcagtacag acagatggca gccctctctg ctgccatttt 420
 cacttcagcc ccaaggtgat gttcaciaag gtactgaagg ccagctgtg ggtgtaccta 480
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 aagattgagc tgcactcacg ctgaggccat tggcagagca tcgacttcaa gcaagtgcta 660
 cacagctggt tccgccagcc acagagcaac tggggcatcg agatcaacgc ctttgatccc 720
 agtggcacag acctggctgt cacctccctg gggccgggag ccgaggggct gcatccattc 780
 atggagcttc gaggcctaga gaacacaaaa cgttcccggc gg 822

<210> 13
 <211> 23
 <212> PRT
 <213> Homo sapiens

<400> 13

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
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Val Ala Gly Pro Val Asp Leu
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<210> 14
 <211> 24
 <212> PRT
 <213> Homo sapiens

<400> 14

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
 1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala
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<210> 15
 <211> 232
 <212> PRT
 <213> Homo sapiens

<400> 15

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
 1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
 65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
 100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
 115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
 130 135 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 145 150 155 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 165 170 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
 225 230

<210> 16
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 <213> Homo sapiens

<400> 16

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Leu Gly
 1 5 10 15

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 20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met

195

200

205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225